

BOOK REVIEW

HANDBOOK OF VENEREAL INFECTIONS

By R. Grenville-Mathers

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It is not clear for whom this book is intended for it is no more than a brief synopsis of the subject, a form of writing which may have value for the purposes of revision but is an unsatisfactory means of acquiring fresh knowledge. Even for revision this publication is not to be recommended. It is very sketchy and superficial and is full of inaccuracies and misstatements. There are also many omissions, and some recommendations with which most venereologists will disagree. Space does not permit a detailed enumeration of errors and omissions because there are so many, but a few typical examples will suffice. It is, for instance, incorrect to say that all reports of the use of penicillin in cardiovascular syphilis "stress the severe Herxheimer reactions which have resulted." It is contrary to general ex-

perience that Herxheimer reactions are "very rare" with the treatment of early syphilis with penicillin suspended in oil and beeswax, and misleading to say that such reactions, when they occur, follow the "first few injections." In discussing sulphonamide therapy there is no reference to renal complications and their prevention; and for treatment with gonococcal vaccine an alarming initial dose of 5,000 million organisms is recommended. The procedure suggested for the treatment of prostatic abscess, namely "passing a metal sound or catheter which evacuates pus into the urethra or . . . incision of the prostate through a urethroscope," sounds potentially disastrous. In a discussion of neurosyphilis it is stated that the span of life used to be only two to two and a half years. Possibly the author meant to write "general paralysis," but in fact he wrote "neurosyphilis." These examples could be extended almost indefinitely. The sum total of the evidence which they give indicates that much of this book needs to be re-written before it can be recommended to those in search of knowledge. A.J.K.

ABSTRACTS

(This section of the JOURNAL is published in collaboration with the two abstracting journals, *Abstracts of World Medicine*, and *Abstracts of World Surgery, Obstetrics, and Gynaecology*, published by the British Medical Association. The abstracts are divided into the following sections: syphilis (general, therapeutic, pathology); gonorrhæa (general, therapeutic, pathology); other venereal disease conditions; public health. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. All subsections will not necessarily be represented in each issue.)

SYPHILIS (General)

II. Attendance Record of Patients Treated by Private Physicians. AIKEN, R. B. (1947). *J. vener. Dis. Inform.*, 28, 224.

The Public Health Department of the State of Vermont supplied penicillin in oil-beeswax (P.O.B.) free of charge to private practitioners for the treatment of 101 white patients suffering from early syphilis. The patients were informed that this treatment was for research purposes and were urged to attend daily for 8 days. Though the stipulated course consisted of 600,000 units daily for 8 days, 15 of the 101 patients were, in fact, treated according to other schemes. Of the 86 patients receiving the recommended course, 70 completed treatment in 8 consecutive days, 1 lapsed without completing treatment, while a further 15 finished their course, though interrupted, in 11 days or under. Broken treatment was due in 5 cases to toxic reactions, in 6 to "personal reasons," and in 4 to the fact that the doctor's office hours were not convenient. G. L. M. McElligott

The Prognosis of Syphilitic Aortic Insufficiency. READER, G. G., ROMEO, B. J., WEBSTER, B., and MCDERMOTT, W. (1947). *Ann. intern. Med.*, 27, 584.

This is a report of the clinical management, over several years, of 43 patients with cardiovascular syphilis. Syphilitic aortic insufficiency may be latent and symptomless for many years. Even with the onset of symptoms the working power of the patient may last for years rather than months. The prognosis is greatly improved by adequate anti-syphilitic treatment. Digitalis and mercurial diuretics should be given when congestive failure threatens. A prolonged circulation time and a low diastolic pressure offer the best index of prognosis. G. F. Walker

Some Remarks on the Importance of the Reactions of the Body in Venereal Diseases. PRAKKEN, J. R. (1948). *Urol. cutan. Rev.*, 52, 406.

Syphilology in France, 1940-47. (La Syphiligraphie Française en 1940-47. VAN LIERDE, L. (1948). *Rev. méd. Louvain*, 16, 252.

SYPHILIS (Therapeutic)

The Relative Antisyphilitic Activity of Penicillins F, G, K, and X and of Bacitracin, Based on the Amounts Required to Abort Early Syphilitic Infections in Rabbits. EAGLE, H., and FLEISCHMAN, R. (1948). *J. Bact.*, **55**, 341.

By employing a method based on the fact that a relatively minute amount of treatment suffices to terminate syphilitic infection in rabbits if it is administered soon after inoculation and before the appearance of the chancre, the authors have evaluated the relative anti-syphilitic activities of penicillins F, G, K, and X and of bacitracin within 2 to 3 months instead of the usual 9 to 12 months.

All the rabbits were inoculated intradermally with 2,000 *Treponema pallidum*, and treated 4 days later by intramuscular injections of the material to be tested, repeated once daily for 4 days. The doses of penicillins F, G, K, and X and of bacitracin that aborted infection in half the animals were 3.5, 0.3, 2.6, and 2.2 mg. per kilo and 90 units per kilo respectively. For penicillins F, K, and X these represent relative activities of 8, 12, and 14 respectively, that of penicillin G being taken as 100. Not only the absolute but also the relative anti-syphilitic activity of the several penicillins and of bacitracin varies widely according to the method of assay. For crude bacitracin containing 30 units per mg., the corresponding activity would be 10% that of G, and for a preparation containing 90 units per mg. (if bacitracin can be purified to that extent) the percentage activity would be 30. Thus, penicillin G was by far the most effective antisyphilitic agent. By the three methods of assay used, penicillin F was 7% to 31% as active as G; K was <6% to 23%, X was 9% to 34%, and bacitracin at 30 units per mg. was 4.6% to 10% as active.

T. Anwyl-Davies

Three Years of Penicillin Alone in Neurosyphilis. STOKES, J. H., STEIGER, H. P., and GAMMON, G. D. (1948). *Amer. J. Syph.*, **32**, 28.

This is the fourth in a series of reports from the University of Pennsylvania on the results of third-year treatment with penicillin alone of 361 cases of neurosyphilis. The first 39 cases have done well: in 64% fluids are normal or nearly normal, and in 82% they are much improved. The findings in spinal fluid have improved in 61% of cases of general paresis; 61% of tabo-paretics; 75% of tabetics; 73% of cases of meningo-vascular syphilis; and 77% of asymptomatic neurosyphilis. Only in 14 of 317 cases are the findings in spinal fluid worse.

The 179 cases in 1946 are classified as cases of "total improvement" and "marked improvement"; the figures for "total improvement" are much the same as those for the previous year: paresis, 63%; tabo-paresis, 63%; tabes, 60%; and meningo-vascular neurosyphilis, 79%. "Marked symptomatic improvement" occurred in the following proportions: paresis, 46%; tabo-paresis 45%; tabes, 33%; and meningo-vascular neurosyphilis, 7%. The proportion of cases in the "marked improvement" group has increased so decidedly in the last year that it seems possible that penicillin therapy, like malaria therapy, causes "a long period of cumulative improvement after treatment is begun or stopped." Thus in tabo-paresis only 13% of patients were "markedly improved" in 1945, and only 17% of those with meningo-vascular syphilis. Usually the degree of improvement obtained by one course of penicillin is not much changed

by additional courses. Nevertheless, some patients improve with second and third courses.

The response to penicillin is usually most pronounced in the first 120 to 200 days; it appears more effective in dealing with abnormalities in the spinal fluid than with symptoms. Its good effect, however, continues through all the stages of neurosyphilis from asymptomatic neurosyphilis to paresis. In paresis, penicillin alone produces almost as good a response as malaria in the second year and the results are equally good in the third year of observation. Symptomatic improvement is as good with penicillin and the action on the cerebrospinal fluid is better. Similarly, in tabo-paresis and meningo-vascular neurosyphilis the improvement in cerebrospinal fluid under penicillin treatment surpasses that obtained with malaria therapy, and the clinical improvement is equal. In tabes, the clinical results are one-third better than those with malaria in the second and third years, and the percentage of normal spinal fluids is twice as high after penicillin treatment as after malaria in the same period. Among 65 patients with lightning pains, 35% showed no change and 38% were much improved.

Herxheimer reactions may cause serious damage, and even 10,000 units is a high dose at the start; doses of 500 units rising to full dosage in 4 to 5 days are being tried. Cardiovascular syphilis complicating neurosyphilis must not at first be treated with full doses of penicillin. The authors are testing the effect of total doses of 9.6 mega units of aqueous penicillin, by giving 40,000 to 80,000 units every 2 hours for 10 to 20 days.

T. Anwyl-Davies

Penicillin Treatment of Neurosyphilis. A Study of Forty-five Cases that had Previously Received Chemotherapy. BARKER, L. P. (1948). *J. invest. Derm.*, **10**, 169.

This report describes the changes in the cerebrospinal fluid which followed the penicillin treatment of 45 cases of neurosyphilis. An aqueous solution of sodium penicillin was injected intramuscularly every 3 hours, the period of administration varying from 18 to 21 days and total dosage ranging from 8 to 12 mega units. All the patients had previously received more than 15 arsphenamine and at least 15 bismuth and mercury injections, the majority having had many more. Some had also had tryparsamide, while several, at least 2 years before, had been given fever therapy. As a result, apart from the Wassermann reaction only in a few cases were abnormalities present in the C.S.F. when penicillin was given. Eight patients had a pleocytosis of 12 to 88 cells, and the count reverted to normal within 6 months after penicillin. Of 19 cases, a high total protein content returned to normal in 10 cases within 6 months, in 13 within 12 months, and in 14 within 18 months. In a further 3 cases the total protein level was still falling at 18 months. Only 5 patients had abnormal colloidal gold curves; all were paretics with changes in the first zone. Three curves became normal 12 months after penicillin while there was little change in the other two 12 to 18 months after penicillin. The Wassermann reaction in the C.S.F. became normal in 27 patients (60%), in 12 (26.6%) the titre declined, and only in 6 (13.4%) was there no response. This effect was considered remarkable in view of the former chemotherapy which these patients had received. Greatest improvement in the C.S.F. occurred in the first year after penicillin treatment and was independent of the amount of previous

chemotherapy; the more recent the infection the greater was the improvement.

S. M. Laird

A Second Report on Intrathecal Penicillin in Central Nervous System Syphilis. THRASHER, J. R., GOSMAN, J., and BOWMAN, G. W. (1948). *J. Indiana med. Ass.*, 41, 216.

Though it is the considered opinion of the majority of British and American syphilologists that intrathecal injections of penicillin are no more effective in neurosyphilis than are the usual parenteral ones, the authors do not agree, and in this article make the following statements: (1) that intrathecal penicillin has given better results than intramuscular penicillin; (2) that intrathecal penicillin with intramuscular penicillin is better than intrathecal administration alone; (3) that the combination of intrathecal and intramuscular penicillin with malaria has, in their experience, given the best results to date. The average intrathecal dose was 20,000 units given at weekly intervals, the recommended initial dose being as low as 5,000 units. The authors have found that large initial doses, especially in acute cases, are liable to be followed by severe reactions. Thirty-five to 45 ml. are withdrawn and reintroduced by the gravity method mixed with penicillin dissolved in saline. The authors have treated 421 cases since August, 1944. [Though the figures in percentages show encouraging results they do not seem to be better than those of Dattner and his colleagues at Bellevue Hospital, who consider that parenteral penicillin alone may well prove to be the optimum treatment for neurosyphilis of all types.]

G. L. M. McElligott

Treatment-failures Following the Use of Penicillin in Late Syphilis. REYNOLDS, F. W. (1948). *Amer. J. Syph.*, 32, 233.

Cases in which penicillin has failed to cure late syphilis may be divided into: cases of resistance, cases in which there is progression in spite of treatment, recurrent cases, and cases in which new lesions develop. Two instances of resistant gummatous syphilis are quoted from the literature, but clinical progression in spite of penicillin is discussed in greater detail. In 6 out of 82 patients with asymptomatic neurosyphilis, 6 out of 24 with paresis, and 6 out of 33 with tabes dorsalis there was failure from this standpoint. Three cases in which bone gummata or cutaneous lesions recurred after penicillin treatment for late benign syphilis are described. Another patient was found to have cardiovascular syphilis with aortic regurgitation 16 months after a course of 8 mega units of penicillin. In all these conditions, and also in primary syphilitic optic atrophy and Erb's spastic paraplegia, penicillin is not recommended as the sole treatment, and the author draws attention to the fact that he has obtained better results in cases of general paresis by combining penicillin administration with fever therapy.

R. R. Willcox

Gastroscopic Observations in Secondary Syphilis. SCHWARTZ, I. R. (1948). *Gastroenterology*, 10, 227.

Twelve patients suffering from secondary syphilis with skin lesions and mucous patches on mouth or pharynx underwent gastroscopy before and after treatment with 2.4 million units of penicillin. In 7 cases there were areas of reddening and oedema in the gastric mucosa with submucosal bleeding and some erosions, and in 4 of the remaining cases similar but less intense changes. In 10 of the 12 cases examined within 3 days

of the cessation of penicillin treatment gastric mucosa was completely normal. In 3 control cases examined before and after penicillin treatment no change in the mucosal appearance followed the treatment. Hypochlorhydria was found in 9 cases before treatment, and persisted in 4. Sigmoidoscopic examination revealed tiny mucous patches in the lower rectum in 6, and in these *Treponema pallidum* was found in 3.

Thomas Hunt

Surgical Treatment of Syphilitic Primary Atrophy of the Optic Nerves (Syphilitic Optochiasmatic Arachnoiditis). BRUETSCH, W. L. (1947). *Arch. Ophthalm.*, Chicago, 38, 735.

An historical survey is given of the hypotheses of the causation of syphilitic primary optic atrophy. Recently the atrophy has been attributed to mechanical distortion of the optic nerves by arachnoidal adhesions. This theory has been proved erroneous by careful investigation of post-mortem material. Of the cases described, necropsy in 1 showed adhesions distorting the optic nerves and chiasma, but, as in the other cases, there was microscopical evidence of a well-marked interstitial neuritis. The author considers that surgical removal of the adhesions is of little value: in all the cases except 1 the adhesions, when present, did not interfere mechanically with the optic nerves; and the basic lesion was an interstitial neuritis which would obviously be unaffected by any surgical procedure. It is stated that the most efficacious treatment of this condition is malarial therapy combined with large doses of penicillin.

G. F. Rowbotham

Icterus in Syphilitics Treated with Arsenobenzenes. (Les icteres des syphilitiques traités par les arsénobenzènes.) GYÖRGY, E. (1947). *Ann. Derm. Syph.*, Paris, No. 11, 433.

The author distinguishes three types of icterus occurring in the early stages of syphilis: (1) syphilitic icterus, which is rare in the serum-negative primary stage, but commoner in the secondary stage; (2) arsenical icterus, which may develop during, or up to 2 or 3 months after, treatment; breakdown products of arsenobenzene may be the cause; contributory factors may be starvation, chronic stomach, or biliary disorders, excessive alcohol, pregnancy, and infectious diseases such as dysentery and malaria; (3) icterus superimposed on syphilis (infective hepatitis). Cases of icterus recently seen in the dermatological clinic of the University of Budapest appear to belong to the third group. Between Aug. 15, 1945, and Dec. 31, 1946, of 1,831 new patients 123 became jaundiced during treatment (77 men and 46 women). Of 702 patients with early syphilis treated with arsenobenzene 20.7% of the men and 13.8% of the women were affected. There was no comparable increase in incidence of jaundice in clinics in other towns. The epidemic was apparently unrelated to dietary deficiency because the number of cases increased while the food situation was improving.

James Marshall

Protective Action of Vitamins C and P against Dichlorophenarsine Hydrochloride (Clorarsen). FRIEND, F. J., and IVY, A. C. (1948). *Proc. Soc. exp. Biol.*, N.Y., 67, 374.

Adult female white mice received an intravenous injection of an LD 85 dose of dichlorophenarsine hydrochloride and were treated for 9 days before and 3 days after the arsenical injection with a mixture of hesperidin

and ascorbic acid. Large groups of animals were employed in both the experimental and control groups. Significant protection was achieved with the vitamin therapy, and the authors conclude that patients should be provided with an abundant supply of vitamins P and C for several days before and during treatment with arsenicals.

G. R. Cameron

SYPHILIS (Pathology)

A Quantitative Precipitation Test for Syphilis. ORPWOOD PRICE, I. N. (1948). *J. clin. Path.*, 1, 91.

Preliminary experiments showed that for the manufacture of a suitable antigen for Price's precipitation reaction (P.P.R.) cholesterol was not necessary; wet ox heart extracted with absolute alcohol proved satisfactory. Fresh wet ox heart is stripped of fat, cut into small pieces, and ground in a mortar with a small amount of absolute alcohol and glass powder; alcohol is added in the proportion of 5 ml. of alcohol to 1 g. of heart, and the whole placed in a stoppered bottle at room temperature for 3 days, the bottle being shaken 2 or 3 times each day. The extract is filtered, placed in the refrigerator at 4° C. for 24 hours, and refiltered. The precipitation titre is found by adding to 0.4, 0.6, 0.8, and 1 ml. of saline 1-ml. amounts of the extract; the containers are allowed to stand for 30 minutes and are then centrifuged; the supernatant fluid is poured off and the tubes inverted for 5 minutes to remove excess of fluid; 0.6 ml. of saline is added to each precipitate and the whole thoroughly mixed. One volume of each of the antigens is added to 3 volumes of (a) moderately positive serum, (b) normal serum, and (c) saline, the tubes are well shaken, and 1 ml. of saline is added; results are read with a $\times 6$ lens and a slit-lamp. The mixture containing the least amount of saline which shows no precipitate with saline or normal serum but a precipitate with positive serum, is the optimum; in practice this has always been found to be 0.6 ml. of saline to 1 ml. of extract.

For the test proper, saline and extract are mixed according to the titre and allowed to stand for 30 minutes; the precipitate is resuspended as above and stored in the ice chest at 4° C. in a brown glass bottle with a glass stopper, where it will keep for months; to prevent infection, 6-8% sodium azide, in the proportion of 0.022 ml. per ml. is added. Sera are inactivated at 56° C. for 30 minutes and a screen test and a quantitative test carried out. For the former, two tubes are employed for each serum, one containing 5 volumes of 50% serum and the other 5 volumes of neat serum: to each tube is added 1 volume of antigen and the tubes are shaken and read as already described. Positive sera—that is, those showing particles—are then subjected to the quantitative test, being tested as neat serum and as serial dilutions from 1 in 2 to 1 in 128. The highest dilution giving the lowest positive reading is noted, and the result is calculated in units by multiplying the dilution by 5. Cerebrospinal fluid is tested, without heating, in a similar way.

In a comparison between P.P.R., the Wassermann test, and the Kahn test, 2,936 sera were examined. There was agreement in 2,817 (95.9%) and disagreement in 119; it appears that the PPR is at least as sensitive as the Wassermann test and rather more specific than the Kahn test. [For an analysis of the serum test results, and for details of a simple and rapid method of carrying out the P.P.R. on large numbers of specimens, the original should be consulted. It seems remarkable that the addition of cholesterol should not have increased the sensitivity of the antigen.]

T. E. Osmond

Development of a Single Standard Slide Test for Syphilis.

KLINE, B. S. (1948). *Amer. J. clin. Path.*, 18, 185.

The author discusses the desiderata for elaborating a standard test for syphilis, which should have maximum specificity, sensitivity, uniformity of results, simplicity, and rapidity. He considers that cardiolipin should form the basis of the antigen, and that it should be mixed with lecithin in the proportion of 1 to 9 or 10, or 1 to 6.5, or 1 to 25; the addition of cholesterol enhances the sensitivity by converting the globular antigen particles to larger needle or plate-like units; an electrolyte such as sodium chloride increases sensitivity by depressing the electronegative charge of the antigen particles. Water is necessary to disperse the antigen particles and should have a pH of 6 to 7; buffers to counteract acid and other positive ions may be helpful, alcohol may or may not be essential, and glycerol increases the flocculating capacity of the antigen and facilitates the reading of results. For the test proper, serum should be heated to 56° C. for 15 to 30 minutes or to 60° to 63° C. for 3 to 5 minutes; 0.05 ml. of serum is the optimum amount and the amount of antigen emulsion should be about one-seventh of this: mixing chambers should have a diameter of 14 mm. and rotation should be at the rate of 180 per minute. Results are read at a magnification of 100; if zone reactions occur dilution should be carried out with 1, 3, or 15 parts of saline or negative serum; the titre of a syphilitic serum is the highest dilution giving a 2 plus reaction. The test would need to be modified in some [unstated] way for testing spinal fluids. It is thought that a flocculation test is to be preferred to a complement-fixation test (C.F.T.), because only two reagents are required as against five and it takes less time, and that a slide test is preferable to a tube one.

[The reply to these assumptions is that "it all depends"; in a well-equipped laboratory under the charge of an experienced pathologist and where large numbers of specimens are tested a batch of 150 to 200 sera could be tested more rapidly (by Donald's dropping technique) by the C.F.T. than by a flocculation procedure; moreover, the same number of tube tests could be completed more rapidly than slide tests. When, on the other hand, only a very few tests are carried out, the flocculation procedure is much quicker than the C.F.T. As regards specificity, much depends on the antigen, and there seems no *a priori* reason why a C.F.T. should not be as reliable as a flocculation test.]

T. E. Osmond

Cardiolipin Antigens in Serologic Tests for Syphilis.

GIORDANO, A. S., CULBERTSON, C. S., and HIGGINBOTHAM, M. W. (1948). *Amer. J. clin. Path.*, 18, 193.

These authors tested large numbers of sera by the Venereal Disease Research Laboratory method with cardiolipin antigens in parallel with the Mazzini microflocculation test. As a rule the cardiolipin-lecithin ratio was 1:9. An analysis of 24,085 tests shows that there was agreement between the two tests in 97.02%, partial agreement in 2.56%, and complete disagreement in 0.42%. Of the 102 cases in which there was disagreement the clinical details suggest that in 8 of the cardiolipin tests and 13 of the Mazzini tests there were false positive reactions, whereas in 62 of the former and 7 of the latter there were true positive reactions; in 12 cases no conclusions could be reached. In the doubtful and negative groups the cardiolipin test gave three times as many false doubtful results as the Mazzini, but 20 times as many true doubtful results. In a second

series of 5,034 sera two cardiolipin antigens with a cardiolipin : lecithin ratio of 1 : 8 were compared : very close agreement was obtained, disagreement being noted only in 3 cases (0.06%). In a third series pooled positive sera in increasing dilutions were tested by the two methods ; 5 cardiolipin antigens gave a pronounced uniformity of results and all were rather more sensitive than Mazzini antigens. It is concluded that cardiolipin antigens are highly sensitive and satisfactorily specific : moreover, they can be reproduced accurately and so lend themselves to standardization.

T. E. Osmond

Cardiolipin Blood Tests in Syphilis. ANDUIAR, J. J., ANDERSON, M. M., and MAZUREK, E. E. (1948). *Amer. J. clin. Path.*, 18, 199.

The theme of this article is that cardiolipin is an advance on all other antigens but that the best use has not yet been made of it. A total of 24,609 sera were examined by two or more of a series of tests including standard Kline and Kahn flocculation tests with and without cardiolipin, and the Kolmer complement-fixation test with ordinary and cardiolipin antigens. The results with varying proportions of cardiolipin and lecithin in 24,381 tests are compared with the results in a similar number of regular Kline exclusion tests ; it is considered that there was a fairly close correlation between the two types of antigen, especially when the lecithin : cardiolipin ratio was about 9 : 1 or 10 : 1 [the critical reader will, however, hardly agree with this, because when the ratio was 9.4 : 1 the regular test gave 103 positive results against 67 with the cardiolipin]. The results are also given of different tests on 17,137 sera from patients in various stages of syphilis and some who were probably non-syphilitic. In general, cardiolipin proved more sensitive than other antigens in both flocculation and complement-fixation tests. As regards false position reactions, 180 tests with the various methods showed that cardiolipin does give such reactions but less frequently than most antigens, though it gave as many in such conditions as acute infectious lymphocytosis, brucellosis, or Vincent's angina. It appears that cardiolipin may continue to give positive reactions in old and treated syphilitic cases almost indefinitely, or at any rate long after all other tests are negative. It is concluded that cardiolipin is easier to work with, is more sensitive and specific, is stable, and yields a reproducible emulsion. Sponsored universal tests based on cardiolipin are urged.

T. E. Osmond

Clinical and Serologic Evaluation of 27,103 Consecutive Slide Tests with Cardiolipin-Lecithin Antigen and Kline Antigen. LEVINE, B., KLINE, B. S., and SUESSENGUTH, H. (1948). *Amer. J. clin. Path.*, 18, 212.

This article reports the results of 27,103 slide tests carried out with cardiolipin-lecithin antigen and Kline exclusion and diagnostic antigens. The optimal ratio of cardiolipin : lecithin is between 1 : 9 and 1 : 10. In a previous report cardiolipin had been shown to give far fewer positive reactions in malaria than did the Eagle, Hinton, Kahn, Kline, and Mazzini tests. Cardiolipin gave 0.0025% positive and 0.2% doubtful or weakly positive reactions as against 0.27% and 0.59% with the Kline diagnostic test and 0.93% and 1.13% with the Kline exclusion test in 24,511 non-syphilitic sera. It gave 1 positive reaction in 56 cases of infectious mononucleosis, 1 in 247 of viral pneumonia, 1 in 513 of jaundice, and none in 4,313 pregnant women ; it also gave none in a number of other conditions including diabetes, coronary occlusion, abortion, rectal abscess,

and herpes [the figures in the text do not agree with those in the table, but the meaning is clear]. In the case of syphilitic sera cardiolipin was rather more sensitive than Kline exclusion antigen and much more so than Kline diagnostic antigen, over 2,000 sera being tested in each series ; this was also the case in 5 newborn children of syphilitic mothers and in a treated case of syphilis where the cardiolipin reaction remained positive much longer. [Many readers will hardly agree with the statement that "no greater specificity (7 false positives in 24,877 non-syphilitic sera) in a test for syphilis is likely to be achieved.]

T. E. Osmond

The V.D.R.L. Slide Test. A Comparison with the Mazzini, Kahn, and Kolmer Tests for Syphilis. WIDLOCK, D. (1948). *Amer. J. clin. Path.*, 18, 218.

In the Venereal Disease Research Laboratory (V.D.R.L.) test for syphilis a cardiolipin-lecithin-cholesterol antigen is used in a slide test. This test was done parallel with the Mazzini and Kahn flocculation tests and the Kolmer complement-fixation test on 52,372 specimens. The Mazzini test gave 16.2% of positive reactions, the V.D.R.L. 13.6%, the Kolmer 10.4%, and the Kahn 9.3% ; of 8,425 sera negative to the Mazzini test only 74 (0.8%) were positive with the V.D.R.L. and Kolmer tests. A comparison of the Mazzini and V.D.R.L. tests showed that the latter gave fewer doubtful reactions than the former. Of 7,409 Mazzini "reactors" 60% gave positive reactions with all the other three tests ; the remainder were negative to one or other of the three tests, the percentages being : Kahn 33.9, Kolmer 26.4, and V.D.R.L. 3.5. It is evident that the V.D.R.L. test approaches the Mazzini (which is essentially a screen test) in sensitivity, and is far ahead of the Kolmer and Kahn tests. [Nothing is said about its specificity, which was not the object of the above investigation.]

T. E. Osmond

Verification Antigen for the Identification of Pseudo-syphilitic Reactions of Serum. HECHT, H. (1947). *Amer. J. clin. Path.*, 17, 949.

The various verification tests so far evolved have proved unsatisfactory ; a good verification antigen should give negative results with syphilitic sera and positive results with certain non-syphilitic sera. The author prefers the word "pseudosyphilitic" to "false positive," since it signifies that the test imitates a positive test for syphilis but is not caused by syphilis.

A selected group of 200 sera, from a total of 20,000 tested routinely, were studied. All the 200 gave positive reactions with Kline antigen and negative with Pangborn [cardiolipin] antigen. The verification antigens were prepared as follows : (1) Dried powdered pregnant uterus, foetus, decidua, cord, or placenta is first extracted with alcohol, then with petrol ether, and finally with acetone ; the remaining tissue is dried and extracted with distilled water and 0.3% phenol, in the proportion of 10 g. of tissue to 200 ml. of phenol solution, in the incubator at 37° C. for 24 hours ; it is then filtered and kept for 14 days in the refrigerator. (2) Dried powdered tissue is first extracted with petrol ether, next with acetone, and then with alcohol ; further steps are as in method 1. The results of slide tests with Kline and Pangborn antigens and antigens prepared from cancerous tissues, human or ox bile, ox heart, and pig bile are set out in four tables. Those sera which reacted positively with the first two were negative with the verification antigens ; in those cases in which the Kline and Pangborn tests

gave different results, the verification antigen tests gave the same result as the Kline; such sera usually came from pregnant women or patients with neoplasms or acute febrile conditions. Where syphilis coexisted with diseases such as cancer or tuberculosis or with pregnancy, positive results were obtained with all three types of antigen. It is concluded that these verification antigens should be useful in detecting pseudosyphilitic reactions.

[Apparently no tests were carried out on sera from patients with those diseases and conditions which commonly give false positive reactions, such as yaws, leprosy, malaria, infectious mononucleosis, and recent vaccination.]
T. E. Osmond

Serum Proteins in Syphilis. Electrophoretic Study.

BENDITT, E. P., and WALKER, S. A. (1948). *Amer. J. Med.*, **4**, 663.

This study was undertaken to re-examine the electrophoretic pattern changes in syphilis, and to investigate the value of such changes as a guide to diagnosis and the effects of treatment. Sera were obtained from: (1) patients in whom syphilis had been diagnosed on evidence other than serological; (2) patients in all stages of the disease; and (3) both treated and untreated patients. Control sera from healthy persons who had not had recent acute infections were also obtained. Four ml. of serum was dialysed against 2 litres of buffer for a minimum of 48 hours at 4° C. The buffer was composed of 0.1 mol. of sodium diethylbarbiturate, and 0.02 mol. of diethylbarbituric acid per litre of solution. At the end of dialysis the serum was diluted to 12 ml. by addition of buffer. Electrophoresis was carried out in a double section Tiselius cell.

Determinations were made on 12 normal human sera, 5 from males and 7 from females. It was found that the concentrations of α -1 and β -globulins were slightly lower in the females. In untreated syphilis the most striking change was the fall in albumin. This was apparent in the primary stage, and persisted through the secondary and tertiary stages. The α -1 globulin level deviated from the normal only in secondary syphilis, in which it was elevated. The α -2 globulin was increased in both secondary and tertiary untreated cases. β -globulin was not significantly altered in any stage of the untreated disease. In all stages of untreated syphilis the γ -globulin was significantly elevated. Total protein concentration did not vary significantly from the normal at any stage of the disease. Treated cases of secondary and tertiary syphilis showed only insignificant changes from the normal in their electrophoretic serum components.

Two patients with primary syphilis in the untreated group gave negative serological reactions. One of them had a normal electrophoretic pattern, the other showed marked changes of the characteristic type. The latter patient also had a chancroid, which may have influenced the pattern. In treated patients with positive serological reactions there was generally no significant deviation from the normal. Three sera from cases of congenital syphilis were studied. Two of these were from treated patients and one from an untreated patient. There was no deviation from the normal. Sera were obtained from 3 persons who gave positive serological reactions at the time the sera for electrophoresis were collected. These were all declared non-syphilitic on clinical evidence after a follow-up of 1 year; in each case the Wassermann reaction eventually reverted to negative spontaneously. The patterns deviated from the normal mainly in that there were low albumin values.
R. B. Lucas

Finding of *Treponema pallidum* on the Clinically Normal Tonsil in Primary Syphilis. (La ricerca del *Treponema pallidum* sulle tonsille, clinicamente indenni da manifestazioni specifiche, di sifilitici in periodo primario.) PASINI, C. (1948). *Arch. ital. Otol.*, **59**, 1.

The author studied the persistence of *Treponema pallidum* on the clinically unaffected tonsil. Mention is made of the discovery of the treponema in an atrophic and pigmented patch at the site of an old lesion in a baby with congenital syphilis, and in sweat glands in the clinically healthy skin of a congenital syphilitic. Hoffmann and Krulle found the organism in the tonsil during the clinically latent stage of syphilis. Other authors have found the treponema in the cervix uteri and in the urethra.

The present work was suggested by Hoffmann's claim that his simple method of obtaining *T. pallidum* from the tonsil even in the serologically negative stage gave results comparable to those obtained from puncture of the lymph nodes. Hoffmann gave a gargle of normal saline, then a mouth wash of dilute alcohol followed by peroxide; he then took scrapings of the tonsil with a sharp spoon and immediately examined them by the dark-ground method. Alcohol was used to remove other spirochaetes which obscured the picture. The present author has not used alcohol, and has relied on his knowledge of the morphology of the organisms. He also stained preparations by impregnation methods and by Giemsa stain. The results in 25 serum-negative and 16 serum-positive cases are presented in two tables. Results were positive in 8 of the serum-negative and in 7 of the serum-positive cases. Although the number of examinations is too small for statistical analysis, the general impression is that a positive result is more likely in the presence of a complicating non-specific lesion of the pharynx.
S. A. Beards

The Action of Bacitracin and Subtilin on *Treponema pallidum* in vitro and in vivo. EAGLE, H., MUSSELMAN, A. D., and FLEISCHMAN, R. (1948). *J. Bact.*, **55**, 347.

This is the first report on the activity and comparative potency of bacitracin and subtilin, two antibiotics prepared from culture filtrates of *Bacillus subtilis*, in the treatment of syphilis. Both were lethal to *Treponema pallidum*, bacitracin much more actively so than subtilin, in vivo as well as in vitro. The unit of bacitracin used was the "amount which when diluted 1 in 1,024 in a series of two-fold dilutions in 2 ml. of beef infusion broth, completely inhibits the growth of a stock strain of Group A haemolytic streptococcus when the inoculum used to seed the tubes is 0.1 ml. of a 10⁻² dilution of an overnight culture in blood broth." The activity of subtilin was expressed in mg., and crystalline penicillin G was used for comparison.

With inocula of 100 *Treponema pallidum* per ml., 0.004 John-Meleney unit of bacitracin per ml. and 0.0047 μ g. of penicillin per ml. completely inhibited growth, so that crystalline penicillin G was three times as active as crude bacitracin, containing 30 units per mg. Pure bacitracin may be at least twice as active. Subtilin was only 1/70 to 1/100 as active as penicillin G, and only 1/20 to 1/30 as active as a preparation of bacitracin containing 30 units per mg. Experiments to establish the rate at which the treponemata were killed showed that, unlike penicillin, there was no maximum effective concentration of bacitracin. The rate at which the organisms were killed increased with the concentration of bacitracin up to the highest level tested (64 units per ml.); at that concentration 99.9% of the organisms were killed in

under 6 hours, compared with an average of 26 hours required by maximum effective concentrations of penicillin. With 0.025 unit per ml. a definite treponemidal effect was observed within 24 to 48 hours. At concentrations of 0.1 unit, 1 unit, and 4 units per ml., 53, 19, and 14 hours were required to kill 99.9% of the organisms. The treponemidal power of subtilin, like that of bacitracin and unlike that of penicillin, increased with its concentration up to the highest level studied (64 µg. per ml.). At that concentration 99.9% were killed in 5½ hours—that is, 5 times faster than the maximum rate at which these organisms can be killed by penicillin G *in vitro*.

In rabbits infected with 2,000 organisms 4 days before treatment with bacitracin, the syphilitic infection was aborted in half the animals by 90 units per kilo given once daily for 4 days. This dosage was 10 times the similarly effective dose of penicillin G. Subtilin approached penicillin in its potency against *Streptococcus pyogenes*, but was far less active than either penicillin or bacitracin against treponemata *in vivo* or *in vitro*; with the largest doses the latter did not disappear from a chancre in rabbits.

T. Anwyl-Davies

GONORRHOEA (General)

Urethral Stricture: A Pathological Study. BEARD, D. E., and GOODYEAR, W. E. (1948). *J. Urol.*, **59**, 619.

A study is reported of 211 consecutive cases of stricture of the urethra, with special reference to causation and pathology. The investigation of each case included urethral instrumentation, urethrography and examination of pathological specimens. Without urethrography a complete picture of a stricture is impossible. From a urethrogram the exact location, number, length, and calibre of strictures can be accurately ascertained.

Of these strictures 90% were the result of gonorrhoea, 5% followed trauma, 2% were the consequence of periurethral inflammation; and in 3% the cause was undetermined. A majority of the strictures developed in patients between the ages of 30 and 50 years. Of the total patients 66% had gonorrhoea 15 years or more before they first presented themselves for treatment, the average period being 21½ years. In some cases of periurethral abscess and urinary extravasation, thrombophlebitis of the corpus spongiosum develops throughout its entire length. Strictures following trauma or periurethral inflammation form in a far shorter time than those resulting from gonorrhoea, the time interval usually being a matter of a few months. Macroscopically a urethral stricture consists of dense fibrous tissue which involves the corpus spongiosum and extends in Buck's fascia, which surrounds it. In 23 cases the strictures were multiple. Since stricture is a disease of the corpus spongiosum and not primarily of the urethral mucosa, it occurs only in that part of the urethra which is surrounded by the corpus spongiosum—that is to say, the anterior urethra with the exception of the 1 cm. distal to the sphincter urethrae membranacea. The majority are situated in the bulbous urethra. Microscopically, the stricture consists of dense fibrous tissue, the arrangement of which is for the most part circular. Of the complications of stricture, acute retention occurred in more than half the cases. Prostatitis causing definite symptoms complicated about 25%, but in almost every case evidence was found of mild chronic prostatitis which was often symptomless. The next most common complication was peri-urethral abscess, which occurred in 17% of cases. [This useful investigation is carefully reported.]

James Kemble

GONORRHOEA (Therapeutic)

The Treatment of Gonococcal Infection with Micronized Penicillin by Inhalation. TAPLIN, G. V., and THOMPSON, H. T. (1948). *Amer. J. Syph.*, **32**, 124.

A method of administration of penicillin is presented which fulfils the demands for reduction in the number of injections, ease of administration, and prolongation of action. These objectives are attained by the inhalation of micronized penicillin-glucose or penicillin-plasma mixture. Therapeutic concentrations in the blood serum for 20 hours after single inhalation of 200,000 to 300,000 units were produced in 3 patients admitted to hospital for serial estimation of penicillin blood level at 2-hourly intervals. Graphs are reproduced of these serial observations in the 3 cases. In another patient comparative serial observations were made of blood levels after 300,000 units were given by: (1) inhalation, (2) injection in oil and wax, and (3) injection in saline. The results, superimposed in a graph, reveal that up to the eighteenth hour penicillin is present in greater concentration in the blood after inhalation than after oil-wax injection; at the twentieth hour both methods gave the same blood level. Blood levels after injection of penicillin in saline, with the exception of the first 4 hours, were decidedly lower than after the two former methods. The authors treated 25 patients with gonorrhoea [presumably males] by this method. In 4 patients inability to use the inhalation apparatus accounted for failure of treatment. In only one of the patients who used the inhalation apparatus efficiently was a failure recorded. Clinical cure was recorded at the end of 7 days, if at least 2 negative smears and cultures had been obtained. [The standard of tests of cure would fail to satisfy most venereologists in Britain, but the initial results of the method are obviously good. The inhalation apparatus is illustrated but not described. The principles involved and method of administration were reported in *Science*, 1947, **105**, 502.]

V. E. Lloyd

Ambulatory Treatment of Gonorrhea with Penicillin Preparations. Experiences with Various Preparations and Techniques. JACOBY, A., OLLSWANG, A., FREUND, J., and ROSENTHAL, T. (1948). *Amer. J. Syph.*, **32**, 133.

The value of assessing the results of treatment in a large number of cases is well exemplified in this statistical analysis, which deals with the results of some 10,000 cases of gonorrhoea treated at the venereal disease clinics of the New York City Health Department. The treatment given to ambulant patients of both sexes comprised various preparations of penicillin: (1) penicillin in saline to a total of 100,000 or 200,000 units in divided doses, or of a single dose of 150,000 units; (2) water in oil emulsions of penicillin in single injections of 150,000 or 200,000 units; (3) penicillin-oil mixtures containing 150,000 or 300,000 units dispersed in a mixture of "falba" (a proprietary substance) and peanut oil (in a few cases stearic acid was used instead of falba); (4) penicillin to a total of 400,000 units in 4 divided doses given orally every 3 hours. Three preparations were used: alum-precipitated penicillin buffered with 0.3 g. of sodium benzoate, crystalline penicillin G buffered with glycerides and sodium-salts of fatty acids, and crystalline penicillin G unbuffered.

The criteria of cure were the disappearance of clinical symptoms, and a negative result from 3 successive weekly smears and cultures from the urethra and prostate

The Effect of Various Proportions and Dosages of Penicillin in Gonorrhœa

Type and Method	Dosage Units	No. Treated		Cured	
		Men	Women	Men	Women
Aqueous solution :					
3 doses	100,000	396	58	87	83
3 doses	150,000	675	178	86	88
1 dose	150,000	101	16	71	75
Water-in-oil emulsion :					
1 dose	150,000	1,649	511	78	86
1 dose	200,000	1,326	484	80	87
Oily mixture :					
1 dose	150,000	3,517	892	65	84
1 dose	300,000	223	50	94	94
1 dose crystalline ..	150,000	57	10	87	80
Oral tablets :					
Plain	400,000	13	0	46	0
Alum—buffered ..	400,000	92	8	88	75
Lipoid—buffered ..	400,000	86	10	76	70

or urethra and cervix. When treatment was unsuccessful, a double dose of the same preparation was given. Some patients required 3 or 4 repetitions of treatment. In view of the exceptionally large number of cases, it is of importance to note that no instance of penicillin resistance was encountered. Determinations of the blood level of penicillin showed no clear relation to therapeutic efficiency. The authors point out that detectable amounts of penicillin in the blood are not essential to obtain cure in gonorrhœa.

V. E. Lloyd

Hypospray Administration of Penicillin in the Treatment of Gonorrhœa. HINGSON, R. A., EASLEY, E. J., GRAY, A. L., TUCKER, C. B., KIESSELBACH, M. R., PARKHURST, G. E., USHER, G. S., and DAVIDSON, H. H. (1948). *J. vener. Dis. Inform.*, 29, 61.

The "hypospray" administers solutions by jet injection through the skin without a needle. The apparatus employed in this study had a spring pressure of 125 lb. and delivered 0.25 ml. of solution per injection. Three injections—of 50,000, 50,000 and 100,000 units of penicillin G respectively—were given at hourly intervals. Two solutions were prepared for the hypospray containing 50,000 and 100,000 units in 0.25 ml. respectively. Intense local pain, erythema, and œdema, persisting for from hours to several days, resulted from injection of the stronger solution; the last dose was therefore given as two injections of 50,000 units. The biceps, triceps, and deltoid muscles were the sites selected and difficulty was encountered in penetrating the skin of some Negro patients. There was a transient stinging sensation at the time of administration but this was lessened if "metycain" or procaine was added to the hypospray fluid. No other severe effects were noted.

The authors treated 158 patients with acute gonorrhœa by the hypospray and 48 others by similar injections given with an ordinary needle. All were admitted to hospital for 10 days. The patients were not considered cured unless 4 post-treatment cultures were negative. Cure rates exceeded 97% by both methods, there being only 4 failures with the hypospray and one after needle injection. These cases all responded to further treatment.

[This apparatus, when perfected, may prove useful not only in large venereal disease clinics but also whenever treatment is given to large numbers of patients.]

R. R. Willcox

Penicillin in the Treatment of Gonococcal Ophthalmia of the Newborn and of Septic Endophthalmitis. (La penicilina en el tratamiento de la oftalmia gonocócica del recién nacido y en la endoftalmitis séptica.) DALGADO BENAVIDES, E. (1947). *Arch. Soc. oftal. hisp.-amer.*, 7, 1121.

The author states that although penicillin modifies the picture in panophthalmitis, it has no advantages over sulphonamides. Even when systemic administration is combined with subconjunctival, anterior-chamber, and intra-vitreous injections, the results are not better. He has found that the most severe cases of gonococcal ophthalmia improve with repeated irrigations of boiled water and injection of penicillin (5,000 units). After the third injection of penicillin the œdema disappears and the gonococcus is no longer found in the pus.

E. E. Cass

Gonococcal Vaginitis in Children Treated with a Single Injection of Penicillin in Beeswax and Peanut Oil. Report of Twenty Cases. CLARKE, B. G., and EISENBERG, H. H. (1947). *Amer. J. Dis. Child.*, 74, 707.

This paper describes the effects of a single injection of 200,000 Oxford units of sodium penicillin in oil in the treatment of vaginitis in negro children. Altogether 20 patients were treated, but 2 received only 100,000 units. There were no untoward reactions in any case, and cure appeared to be prompt and complete.

Patrick Mallam

GONORRHOEA (Pathology)

Bacteriologic Follow-up of Penicillin-treated Gonorrhœa in Women. HIRSCHBERG, N. (1948). *Amer. J. Syph.*, 32, 141.

Most of the reports on the results of penicillin therapy for gonorrhœa refer to the response to treatment in men. Only a few reports deal with a large series of women patients. Some are based on careful bacteriological studies, but in others no tests have been carried out after clinical cure. The author took the opportunity of observing the results of penicillin therapy over a post-treatment period of 10 weeks in women imprisoned for prostitution. Cases were selected for study only after the isolation and identification of the gonococcus by culture and fermentation tests with specimens from the urethra and cervix. All 54 cases were treated with 150,000 units of penicillin in oil-wax. There were only 2 failures of this treatment. In one the gonococcus was found again 3 weeks after treatment, and again 2 weeks after a second treatment. In the other case a positive culture was not obtained until 7 weeks after treatment. The author considers that cultures at regular intervals after apparent cure are of considerable importance. He also comments upon the larger number of Gram-negative bean-shaped diplococci which might be confused with the gonococcus in stained smears or in cultures when the results are unconfirmed by fermentation tests.

V. E. Lloyd

A Comparison of Twenty-four-hour and Forty-eight-hour Readings of Routine Gonococcus Cultures. MUELLER, A. M., and NELL, E. E. (1948). *Amer. J. Syph.*, 32, 139.

It is often of considerable importance to be able to isolate and identify the gonococcus by culture as soon as possible. The optimum incubation period for diagnostic purposes is usually accepted as 48 hours. The authors

set out to investigate a report that a 24-hour period was as good as or possibly better than the customary 48-hour period. For their purpose they used a medium consisting of 1.3% "difco"-dextrose-starch agar adjusted to pH 7.4. Specimens of discharge and of centrifuged urine were smeared on two plates as soon as possible after collection and incubated in candle jars at 36° C. Examinations were carried out at the twenty-fourth and forty-eighth hours. The positive cultures studied numbered 112; all these were positive at 48 hours but only 58.9% were positive at 24 hours. The discrepancy was considerably more evident in specimens from women (46.1% positive at 24 hours) than from men (86.1% at 24 hours). The amount of contaminating growth was not found to be greater at forty-eight hours, and colonies at the end of that period were better defined and more easily detected. The authors confirm that the customary 48-hour incubation period is the more efficient.

V. E. Lloyd

OTHER VENEREAL DISEASE CONDITIONS

Virulence and Antigenicity of *Hemophilus ducreyi*. DIENST, R. B. (1948). *Amer. J. Syph.*, 32, 289.

Cultures of *Hemophilus ducreyi* became avirulent for rabbits and human beings when subcultured for several months on defibrinated rabbit blood. Lyophilized cultures of freshly-isolated strains remained virulent for rabbits and human beings even after 18 months' storage at room temperature. Virulence for human subjects was tested by placing 0.1 ml. of 48-hour rabbit blood culture on the scarified skin; virulent strains produced "pustulettes" within 72 hours. Three avirulent and 2 virulent strains were selected for testing antigenic power. All five antigens were injected into the skin of 20 known positive and 40 known negative Ducrey reactors. Readings after 72 hours revealed no discrepancy in the reactions produced by the virulent and avirulent strains.

R. R. Willcox

Treatment of Chancroid with Streptomycin. HIRSH, H. L., and TAGGART, S. R. (1948). *J. vener. Dis. Inform.*, 29, 47.

Since Mortara and Saito showed that *Hemophilus ducreyi* was sensitive to streptomycin and that this substance was effective against experimental chancroid, its application to the disease in human subjects was inevitable. The disease was diagnosed in 15 patients by means of positive cultures from sores or buboes which had been present from 7 days to 3 months, or by the recovery of the organisms from smears stained with Pappenheim's stain and a positive Ducrey skin reaction. Three of the patients had previously been treated with sulphonamides and 2 with penicillin, without improvement. All but one, given 2 g., received 1 g. of streptomycin daily in divided 4-hourly intramuscular injections. Treatment was continued until the lesions were healed; this took from 5 to 25 days; in 11 instances they were healed in less than 2 weeks. Buboes were aspirated where necessary and no toxic effects were noted. The follow-up period extended over 1 to 30 weeks, and one possible relapse was observed 6 weeks after treatment was completed.

R. R. Willcox

Penicillin-Procaïne in Acute Parametritis and Salpingitis. (Penicilina-novocaina en las anexo parametritis agudas.) GONZÁLEZ, M. (1947). *Arch. Soc. Ciruj. Hosp.*, 17, 507.

In view of the application of the work of Leriche on procaine block to gynaecological conditions by several

authors, and also of the use in inflammatory conditions of the eye of a procaine-penicillin mixture, the author had employed this mixture in the treatment of a series of cases of acute infection of the parametrium and uterine appendages. He described his technique in detail and the results in 16 cases. In 7 patients who were followed up for 6 months an anatomical and functional cure was obtained, though in 2 cases a second injection was necessary. In 6 cases there was either no follow-up study or the period after injection is short, but in most of these the immediate results were satisfactory. In 3 patients the treatment failed; 2 were operated upon for pyosalpinx, and the third had appendicitis. In this latter case, however, the failure of the injection to relieve pain was considered to be a helpful diagnostic feature. After discussing the various theories about the action of procaine, the author puts forward the view that the two drugs have a synergistic action. This treatment is recommended on the grounds that it is successful, economical, harmless, and simple, and can be carried out on ambulant patients.

Bryan Williams

Genital Manifestations in Early Filariasis. BEACH, E. W. (1948). *J. Urol.*, 59, 371.

This paper is based on experience with a U.S. Naval Medical Unit in the Pacific where filariasis was endemic. Attention was drawn to this disease by the complaints of about 30% of a battalion who had spent about 5 months in Samoa in close contact with the natives. The microfilaria was finally found in the perivascular tissues of a few of the patients after extensive and negative search for it in blood films, excised lymph nodes, and hydrocele fluid. Clinically the first symptoms and signs are of generalized, or sometimes regional, lymphangitis and adenitis. This may be recurrent, leaving obvious fibrosis of vessels and lymph nodes; the inguinal nodes are most commonly attacked; next commonest are the axillary nodes. The recurrent attacks may be allergic reactions to toxins secreted by the adult worm (*Wuchereria bancrofti*) somewhere in the lymphatic system. Elephantiasis is said to be a later form of filariasis, due to lymphatic fibrosis. In the genital system, vasitis or funiculitis is the usual lesion and is mostly unilateral; pain and swelling begin at the inguinal ring and rapidly involve the testicle. When this condition is recurrent there may be considerable thickening and irregularity of the vas, but never so markedly as in tuberculous infection; surgical exposure proves that the lesion is really a perivascularitis, the lumen of the vas being unaffected. Testicular atrophy does not follow these attacks and the general disturbance is minimal. The condition must be differentiated from other causes of epididymitis, varicocele, hernia, torsion of the testicle, hydrocele, and subacute appendicitis. Treatment is unsatisfactory, consisting in the removal of the patient from the endemic area and the giving of quinquivalent antimony.

Hugh R. Arthur

Histological Observations on Gangosa. (Contributo isto-patologico allo studio della gangosa (rino-orofaringite mutilante dei propici).) BETTOLO, A., and LUGO, G., (1948). *Acta med. ital. Mal. infett. parassit.*, 3, 32.

An Arab woman aged 52 stated that 20 years ago a small painless nodule appeared on the left nostril. This soon broke down and the lesion, in spite of many forms of treatment, gradually extended on the surface and in depth until much of the nose, mouth, and face was

destroyed by a typical gangosa. The state of this unfortunate woman is illustrated in a series of photographs. *Mycobacterium leprae*, *Myco. tuberculosis*, *Treponema pertenue*, leishmania, rhinoscleroma, and blastomycetes were repeatedly searched for, but in vain. The Wassermann reaction was on one occasion, in 1939, considered to be positive, but tests over the next 3 years were negative, and the Kahn and Meinicke reactions were always negative. No benefit was obtained from arsenicals, antimonials, mercurials, iodine, bismuth, sulphonamides, and x rays and the patient died. Histological examination of different parts of the local facial lesions and of some of the viscera—lungs, heart, liver, spleen, and kidneys—was undertaken. Brief descriptions are given and photomicrographs reproduced of some of the histological appearances of the tissues of the face—congestion of the vessels, haemorrhages, lymphocytic infiltration, and relative scarcity of granulocytes and plasma cells—but nothing was found which could be regarded as characteristic or pathognomonic. The author sees no reason for regarding gangosa as a sequel to or complication of yaws, and inclines to the view that gangosa is a condition *sui generis* or "a separate clinical entity."

H. Harold Scott

Value of Penicillin in the Treatment of Yaws in Haiti.
(La valeur de la pénicilline dans le traitement du pian, en Haïti.) DUVALIER, F. (1948). *Un méd. Can.*, 77, 17.

Yaws affects 85% of the rural population of Haiti, and as 60% are infected in childhood its non-venereal character and non-hereditary transmission are established. It appears difficult to produce negative serum reactions by any treatment. In this series cases were treated alternately by one of three methods: (1) 200 cases received 1,200,000 Oxford units of penicillin sodium in 30 injections of 40,000 units over a period of 4 days. (2) 151 cases received total doses varying from 600,000 to 1,200,000 units of penicillin calcium in oil in 2 days. (3) 149 cases received 1,200,000 units in 2 doses at 12-hour intervals. Immediate results were "marvellous." No toxic effects, other than fever at the beginning of treatment, were noted. The quicker the "cure," the less effect was noted on the serum reactions. With the first method 105 out of 200 became negative to the Kahn test though remaining positive to the more sensitive Kline, Boerner—Jones—Lukens, Mazzine, and Kolmer tests. With the second and third methods only 3 out of 300 became negative even to the Kahn test. The cerebrospinal fluid appeared normal in the 10 cases studied. The author concludes that 1,200,000 units are insufficient as a cure, though if injected in oil this dose renders possible a preventive campaign on a large scale. Treatment with penicillin combined with prolonged "mapharsen" therapy, as for syphilis, ought to be tried.

Clement Chesterman

PUBLIC HEALTH

Infective Hepatitis in West Africa. FINDLAY, G. M. (1948). *Mon. Bull. Min. Hlth.*, 7, 2.

This study is concerned with both infective and syringe-transmitted hepatitis in European and native troops in West Africa between 1941 and 1945. In West Africa the incidence of infective hepatitis was greatest during the rainy season and almost every tribe was affected. The African proved generally less susceptible than the European, though in the latter 2 out of 413 patients died while in the former 80 out of 1,309 patients admitted to hospital died. Of 62 deaths in Africans, 52 were of men who had served for less than 1 year. This reinforces other evidence that a fatal outcome is likely in the presence of malnutrition. In some outbreaks in civilian villages mortality was much higher (10 out of 32 in one series).

Previous experiments carried out by Findlay and Willcox had shown that the disease could be transmitted by the oral ingestion of faeces. Positive results were also obtained with urine, in contrast to the findings of others. Subsequent investigation showed that the donors employed had suffered from schistosomiasis and that traces of blood were present in the urine. Experiments with European donors gave no results. Thus, in a community where bilharziasis is rife, the urine is a potent source of infection. No experimental transmission was, however, obtained with nasopharyngeal washings.

Since the venereal disease rate in West Africa is one of the highest in the world, and many thousands received arsenical injections for both yaws and syphilis, it is remarkable that there were in 5 years only 19 recorded African cases of syringe-transmitted hepatitis in the venereal disease clinics. Five were fatal. A further 5,000 Africans were treated with intravenous tartar emetic and other antimonials in the course of a single outbreak of schistosomiasis, without such hepatitis being noted. Attempts to transmit the disease by ingestion of faeces and urine failed. Among white troops only 8 cases were recorded, with 2 deaths. Outside the venereal disease clinics there was an outbreak of hepatitis of explosive violence involving 689 Europeans between December, 1942, and January, 1943, and following yellow fever inoculations performed in Britain in October and November, 1942. The ratio of officers to men affected was 1 : 6.35, compared with a ratio of 1 : 1.82 for infective hepatitis. The high incidence of the latter condition amongst officers is attributed to poorer mess hygiene. The incubation period in the outbreak far exceeded the 15 to 40 days in infective hepatitis. Two Africans who were given injections of known icterogenic serum developed hepatitis 85 and 98 days later. The author suggests that the hepatitis viruses should be classified as: (1) infective hepatitis, (2) haematic hepatitis: (a) human; (b) equine.

R. R. Willcox